



How to live better longer?

Why we fail? What to do and avoid? How to succeed?

Dr. med. Ludwig Manfred Jacob



We all want to live better longer!



Seikichi Uehara, 97 years

Wareham retired at the age of 95



Why we fail?

What to do and avoid?

How to succeed?

To understand the nature of health and disease we need to ask: "why?"

Instead of reading and understanding the book of life, science too often just analyses the ink in it.





Why we fail? We used to be hunted by deadly disease!

Today we are addicted to silent killers that kill slow and hurt little:

- 1. High stress, lack of sleep & exercise
- \rightarrow addicted to eating high energy food
- \rightarrow Metabolic Syndrom \rightarrow
- 2. Hypertension, diabetes, CVD and cancer
- 3. burn out, chronic fatigue, depression
- 4. Loss of bones and muscles \rightarrow hip fracture
- \rightarrow loss of independence and social life



What went wrong?

30 km/day 130 km/hour



The **"species-appropriate human nutrition"** from scientific point of view: **"a mixed, but predominantly plant-based diet".** This is demonstrated by the anatomy of the dentition, intestinal length, enzyme expression (e.g. no vitamin C synthesis as in herbivores, poor uric acid degradation) and by the entire history of development.

Which diet leads to the goal?









Energy balance: A question of nutrition?

Too much protein inhibits the energy metabolism (\rightarrow ammonia!)

Pure herbivores

Racehorse Hawkster: 61 km/h at 2414 meters Fastest carnivore



Study on cheetahs (*Nature*): 54 km/h at max. 200 meters



The deadly quartet of civilization diet

Meat products	Dairy	Sugar/ white flour	Salt
+ too much stress		+ too little sleep -	+ excercise

The deadly quartet of metabolic syndrome

Fat depositions in abdomen and liver

Insulin resistance

Dyslipidemia Hypertension



Metabolic Syndrome – the belly grows and grows to be the breeding ground of our life style diseases



We want more and more. And our brain screams for energy \rightarrow evil circle of insulin

Carbs ≠ Carbs explosion vs. Camp fire

Glycemic Index ≠ Insulin-Index Blood sugar effect ≠ insuline effect

Our food are our drugs. Hippocrates: "Let food be your

medicine, and medicine your food."



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Food-Insulin-Index (FII) (Bao, Willet, Brand-Miller et al., 2011)

food (1000kJ)	weight (g)	GI	GL	Insulin-Index
Glucose	59 g	100	59	100
Fruit yogurt	260 g	31	12	84
Skim milk	690 ml	29	9	60
White bread	97 g	70	31	73
Oranges	625 g	42	21	44
Steak	158 g, <mark>0 g CHD</mark>	0	0	37
Pasta al dente	200 g, <mark>49 g CHD</mark>	46	23	29
Tofu	227 g (27 g P, 7 g CHD)	15	1	21
White beans	281 g (19 g P, 28 g CHD)	31	9	23
Steak + potatoes (2000kJ)	52 g P, <mark>40 g CHD</mark>	77	31	86
Pasta with lentils (2000kJ)	27 g P, <mark>63 g CHD</mark>	42	27	45
90 g Pizza/ 600 ml Cola	12 g P, 92 g CHD	55	51	85



Insulin is highly anabolic: it first makes us tall, then obese and finally ill

Fat loaden cells no longer respond to insulin: insulin resistance → chronically elevated insulin levels

Fatty liver \rightarrow central insulin resistance Fatty muscles \rightarrow peripheral insulin resistance

- ↑ Cholesterol,
 ↑ Estrogens,
 ↑ Blood lipids
- ↑ Increase in heart rate and/or blood pressure
- ↑ reward & addictive system in the brain
- \rightarrow \uparrow Diabetes, Cardiovascular diseases

Insulin/ insulin-like growth factor IGF-1 → ↑ cell growth, cell division and cancer



Diabetes due to sausage or pasta?

EPIC study (38,094 participants, 10 years of follow up) : Risk increasing factors for type 2 diabetes:

- 118 % animal protein
- 1 27 % high glycemic load,
- ↑ 15 % numerous carbohydrates
- vegetable protein
- ↓8 % fibre
- (Sluijs et al., 2010a and 2010b)

Meta analysis of the *Harvard School of Public Health* (442.101 participants) :

↑51 % due to 50 g processed meat/ day
 ↓32 % due to replacement of processed meat by nuts
 ↓25 % due to replacement of processed meat by whole grain

↓ 35 % due to replacement of processed meat by whole-grain products (Pan *et al.*, 2011)

High protein consumption (> 20 % of energy) (Levine *et al., 2014):* ↑ 5-fold type 2 diabetes mellitus ↑ 4-fold death from cancer (IGF-1) 18 years later (Analysis of NHANES III study data)



Low-carb diet for health?

Prof. Valter Longo, currently the world's leading scientist in the field of life extension, proves:

Low-carb, high-protein, high-fat diets promote cancer cardiovascular disease and the ageing process via multiple pathways (e.g.IGF-1, MTOR, TOR-S6K, PKA)

"When you look at multidisciplinary studies, you realize that the high-protein, high-saturated-fat, and low-carb diet is one of the worst for your health. Populations with record longevity do not eat this way [...]. Also, if we examine the laboratory studies, we see that both high protein intake and high saturated fat intake are associated with aging and disease [...]."



How Animal-based and Heavily Processed Foods Make Us Sick

Analysis of the Physiological, Clinical and Epidemiological Evidence

Causes: Hypercaloric, energy-dense, heavily processed, protein and salt-rich, potassium-poor foods of mainly animal origin, along with sugar and white flour, lack of movement and sun exposure.





Mitochondrial dysfunction: ever more energy production until collapse



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What we put into our mouth, is not transformed into energy.







Acid-base- and mineral balance: Man is the only mammal with high blood pressure!







Hypertension worldwide the killer Number 1 Too much salt, too little potassium (plants)

- The Lancet Global Burden of Disease Study 2010 :
 1. Hypertension 2. Smoking are risk factors for death and invalidity
 - Potassium softens blood vessels, salt stiffens them (Oberleithner *et al.*, 2007 and 2009)
 - Potassium supplements lower risk of stroke in patients with hypertension by up to 64 % (Ascherio *et al.*, 1998)
 - Mortality after 15 years (Yang *et al.*, 2011)
 - ↑ by 20% per 1 g sodium,
 - \downarrow by 20% per 1 g potassium





Na-K-Dysbalance





Post-agricultural inversion of the potassium-to-sodium and base-to-chloride ratios



Diet, evolution and aging--the pathophysiologic effects of the post-agricultural inversion of the potassium-tosodium and base-to-chloride ratios in the human diet (Frassetto et al.) European Journal of Nutrition ·





Acid-base and mineral imbalance damage joints, bones and muscles

Acidosis promotes:

- Inflammatory processes and pain in muscles and joints
- Release of calcium and magnesium from the bones to neutralize free acids → bone loss
- Protein degradation in the muscle \rightarrow muscle loss
- > Risk of falls and bone fractures $\uparrow \uparrow \uparrow$
- Decrease in renal function with age. From latent to real acidosis: bicarbonate buffer \$\p\$, risk of heart attack & stroke \$\p\$

Important is sufficient intake of:

- Calcium and magnesium to compensate for mineral losses
- Potassium for deacidification of the cell interior
- Potassium citrate (not potassium chloride!) neutralizes acid load, prevents calcium degradation from bones and increases bone density

Your bones are essential! Keep them strong! Stop osteoporosis!

- Vitamin K2 (75-180 µg) in synergy with:
- Vitamin D -> sunlight or approx. 1000-2000 IE summer or 4000 IE.
 Winter, check serum levels: 75-125 nmol/l)
- Potassium, magnesium, calcium citrate, Borate, Silizium
- Walk, exercise!
- Adapt home and bathroom to your age!

Falls are a leading cause of disability





Hip Fracture

Stress hormone cortisol: salt accumulates; potassium, magnesium & calcium are lost

- Promotes excretion
 - Of excess acids and nitrogen
 - But also of potassium, magnesium and calcium
- Increases salt retention (sodium+chloride)

For permanent stress:

- Overload with sodium chloride
- Increased loss of minerals (K, Mg, Ca
 - Sufficient intake is particularly important!





Stress makes fat

- Enzyme 11-beta-hydroxysteroid dehydrogenase (HSD) converts inactive cortisone to active cortisol
- Cortisol triggers signal for fat storage
- HSD is mainly found in abdominal fat and liver cells
 - Edema formation
 - Inhibition of metabolism
 - Fat accumulation in abdomen and liver
 - \rightarrow insulin resistance, diabetes



Stress makes angry and sick

- Stress increases release of adrenaline, norepinephrine, cortisol and glucose
- Stress makes breathing flat and fast
 - ↓ Exhalation of acids
 - J Oxygen for energy production
- Consequences of "cold stress": Narrowed blood vessels, little oxygen, lots of sugar
- Cold stress exhausts energy, redox and acid-base balance





Lack of sleep leads to burnout and promotes cancer, obesity and diabetes

- Night work increases cancer risk (Parent *et al.*, 2012)
 - 177% for prostate cancer
 - 127% for pancreatic cancer
 - 103% for colon cancer and 109% for rectal cancer
 - 76% for lung cancer
 - 74% for bladder cancer
 - 131% for non-Hodgkin lymphoma
- Possible causes: ↑weight, ↓immune system, ↓melatonin
- Melatonin: antioxidative, neuroprotective, immunopromoting
- Quadrupled risk of advanced prostate cancer at low melatonin levels (Sigurdardottir *et al.,* 2015)
- For sleep problems: 1 3 mg melatonin





Stopover burnout or depression – Ejecting from the stress spiral



 \rightarrow

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Silent inflammation = silent killer

- Acute (it hurts)
- Chronic and low-grade (it kills)
- Acute inflammation is a normal physiological response critical to maintain homeostatic control, but when it becomes chronic, inflammation contributes to the pathophysiology of all major diseases

Atherosclerosis — An Inflammatory Disease

RUSSELL ROSS, PH.D.

New Eng J Med 1999



THEROSCLEROSIS is an inflammatory disease. Because high plasma concentrations of

Inflammaging and "Garb-aging"



The beneficial effects of MedDiet could be the result of a decreased production of cellular and molecular garbage which is the fuel of aging and inflammaging



Contents lists available at ScienceDirect Ageing Research Reviews



(E) CrossMark

Review

Health relevance of the modification of low grade inflammation in ageing (inflammageing) and the role of nutrition

Philip C. Calder^{a,b}, Nabil Bosco^c, Raphaëlle Bourdet-Sicard^d, Lucile Capuron^{e,f}, Nathalie Delzenne⁸, Joel Doré^h, Claudio Franceschiⁱ, Markus J. Lehtinenⁱ, Tobias Recker^{k,*},

Why are we aging? The ancient concept of slagging/toxin accumulation" proven again

- Aging and age-related diseases due to
 - Chronic stress
 - Microbiota-gut-brain-axis
 - Increased inflammatory state \rightarrow "Inflammaging"
- ,The enemy from within'
 - Inflammaging as autoimmune, autoinflammatory process
- Inflammaging and 'Garb-aging' (Franceschi et al., 2017)
 - Cell debris (cellular garbage)
 - Misplaced and/or misfolded proteins
 - Senescent or apoptotic cells

Inflammaging and 'Garb-aging'

Trends in Endocrinology & Metabolism

Review

Inflammaging and 'Garb-aging'

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Claudio Franceschi,¹ Paolo Garagnani,^{2,3} Giovanni Vitale,^{4,5} Miriam Capri,^{2,3,‡,*} and Stefano Salvioli^{2,3,‡}

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Hippokrates (2500 v.Chr.) - *Corpus Hippocraticum*

The right diet (Diaita) and life style as central therapies: "Fasting purifies body and soul." (→ autophagy) "Let food be thy medicine and medicine be thy food" "We do not live to eat, but eat to live". "Of all our body fluids acids are the most harmful".

Cause of obesity: "feasting and inertia",

Therapy: purely vegetarian food lots of exercise in fresh air and sun Deep sleep

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Inflammaging


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the most underdiagnosed disease

Histamine intolerance

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Inflammation – it all starts with histamine!



FIGURE 1. Summary of histamine-mediated symptoms. Adapted with permission from Maintz L et al. Dtsch Artzebl 2006;103:A3477-83.

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Cancer kills, but it is not just destiny!

cancer number 1 lung cancer \rightarrow smoking cancer number 2 Prostate/breast cancer \rightarrow ??? cancer number 3 und killer no. 2 colon cancer \rightarrow food

Patients with the common low risk prostate cancers do not need invasive treatment.

Choose wisely!

ment.	Low-Risk	Medium-Risk	High-Risk
PSA Level*	Less than 10 ng/ml**	10 to 20 ng/ml	More than 20 ng/ml
Gleason Score (see page 6)	6 or lower	7	8 or higher
Tumor Stage (see page 7)	T1 or T2a	T2b	T2c

First we grow, then our abdomen and glands (prostate, breast) and finally often a carcinoma . . .





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WHO 2000: 27 times higher age-standardized prostate cancer mortality in CH/Sweden/Norway



 Norway, Sweden, Switzerland: high consumption of dairy products, meat and sugar for decades

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- Worldwide high correlation with meat, animal fat, milk, sugar, alcohol (Colli und Colli, 2006)
- Risk of fatal prostate cancer is 3.6-fold increased with high consumption of milk, cheese, eggs, meat (Snowdon et al., 1984)



Milk consumption/prostate cancer

(adapted from Ganmaa et al., 2002)

Milk is not meant for humans: Calves grow 10 x quicker than human babies!

Milk rich in hormones (estrogens, progesterone), proteins and growth factors (IGF-1 ↑ mTor ↑ insulin), calcium, saturated fatty acids, cholesterol.

Bovine Leukemia Virus (cow milk, meat) boosts breast cancer risk (Buehring at al., 2015).

Soy milk reduces pca risk by 70 % (Jacobsen *et al.,* 1998)!

From calf to cow 1-2 years







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Beef consumption Prostate cancer mortality





Outside cancerogenic (e.g.PAKs) inside → thermostable cancer viruses e.g Bovine leucemia virus NCI 2015: Hamburger polyoma viruses Nobel laureat zur Hausen avoids any beef.

More sugar, higher prostate cancer mortality (Colli und Colli, 2006)

Sucrose \rightarrow 1. Glucose \rightarrow \uparrow Insulin \rightarrow 2. Fructose \rightarrow Liver fat \rightarrow \uparrow Insulin resistance \rightarrow Cancer, overweight and diabetes \uparrow \uparrow \uparrow



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It is not too late! Will to change as an opportunity

No doctor knows YOUR prognosis! Doctor as NOCEBO or PLACEBO!

Take control of your destiny!

Genetics \rightarrow My destiny Epigenetics + milieu \rightarrow is in my hand!

GEMINAL pilot study (Ornish et al., 2008) proves:

Cancer genes can be "switched on or off" by diet and lifestyle and thus their effects can be greatly altered.

Success of holistic prostate cancer treatment

- Clinical study with 93 patients (active surveillance)
- At least 2 years longer without invasive therapy: Invasive therapy in 27 % of control group, but only 5 % of Ornish group (- 82 %)
- Pure vegetarian, low-fat wholefood; daily tofu
- Selective use of dietary supplements
- 6 x 30 min. walk per week
- Psycho-spiritual components with stress management: yoga, breathing exercises, progressive muscle relaxation, meditation, visualisation exercises, weekly group session (Frattaroli *et al.*, 2008)

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What is good for your prostate is good for your heart!



\rightarrow Very good Compliance: 71% continue after 5 years!



Plant power against prostate cancer Dr. Jacobs essentials recipes: www.drjacobs.de

- Vegetables, herbs and fruit (8-10 servings a day)
 - All starch-poor vegetables to eat to your heart's content
 - Pomegranate, best fermented (600 mg polyphenols)
 - Healthy drinks: green tea, coffee, organic red wine
 - 30 mg lycopene in approx. 300 ml tomato juice/50 g tomato paste
 - Cruciferous plants (e.g. broccoli sprouts/seeds, cabbage, horseradish), curcumin, garlic, onions, wild garlic, walnuts, linseeds
 - 55-200 µg selenium
 - up to 50 IU vitamin E (vitamin E family)
 - If necessary 1 g DHA/EPA (diet without fish)

All these natural substances neither achieve a safe healing nor replace a possibly necessary curative treatment. 21/06/18

Sports and physical activity

 Health Professionals Study (1990-2008), 2,705 patients with non metastatic prostate cancer

General mortality risk↓ 46% by: > 90 minutes/week or 15 min./day physical activity Walking, jogging, cycling, gardening

- 3 h strenuous exercise / week:

 4 61% prostate cancer mortality
- Do not accelerate from 0 to 100!



Sport halves cancer risk and recurrence rate.



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What to do and avoid?

Looking for role models:





Seikichi Uehara, 97 years



Heart surgeon Dr. med. Ellsworth Wareham retired at the age of 95



Where do the oldest, scientifically investigated people in the world live?



What do the oldest, scientifically investigated people in the world do have in common?

body	 physical activity in everyday life moderate, plant-based diet 	
	3. smoke-free environment	
mind/ emotions	positive relationships: family, friends, job slowed-down life: balance relaxation/activity	
soul	meaning of life religious community love	







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Okinawa: Isle of the Immortals



Seikichi Uehara, 97 years old

"At 70 you are still a child, at 80 you are just a youth, and at 90, if the ancestors invite you into heaven, ask them to wait until you are 100, and then you might consider it."

Highest density of centenarians and supercentenarians

80-90 % lower mortality due to cardiovascular diseases, breast and prostate cancer



What do Okinawans eat?



Healthy living, vegetarian Adventists live 13,2 years longer: almost as long as their wives!

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Vegetarian/vegan Adventists 96,000 participants: much less diabetes, less overweight, less cancer

Adventist-Health-Study II supported by NIH, USDA, and the World Cancer Research Fund International

- Vegans weigh 13,6 kg less than omnivores
- Least hypertension and risk for type 2 diabetes:
- Diabetes risk 4x higher for omnivores compared with Vegans.
- Vegan diet reduces risk of cancers specific to women by 34 %
- Vegan diet reduces risk of prostate cancers by 37 %

Dr. med. Ellsworth Wareham: 95

As a pioneer of heart surgery and heart transplantation the surgeon practiced up to his 95th year of life and feeds on a solely plant-based nutrition since 50 years. In 2014 he turned 100 years old:



Smoker's leg



Aortic cholesterol deposition



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Dr. Jacobs Way

Eat Healthy Food with Delight

Relax with Deep Breathing and Sleeping

Exercise with Joy

No magic bullet: Silent healers against silent killers



The three basic rules:

- 1. Drink lots of healthy, non-caloric liquids.
- Eat your fill of plant foods from all 5 colors always observing food sensitivities. (→ gluten, fructose, histamine intolerance, allergies etc.)
- Choose foods with high micronutrient-density, low energy-density, high potassium and low sodium content.

Most need to supplement vitamin D throughout the year. Vegans and everybody above 50 should supplement B12.







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Dr. Jacobs Way of lasting health

Dr. Jacob's Food Pyramid

Foods



% = per cent by weight

The recommendation (70 % category 1, 30 % category 2) refers to normal and overweight people.

Underweight people should turn this ratio and consume 70 % of category 2, e.g. in the form of nuts and healthy oils. Slim people, who do not want to gain weight, usually can maintain their weight well with 50 %/50 %.

How to succeed? Dr. Jacob's concept: simple, effective, holistic

- 1. The essential basics: supplement what is really missing
 - Supply often inadequate:
 Vitamin D, Vitamin B12, iodine, selenium, potassium, calcium, magnesium, zinc, omega-3-fatty acids
- 2. Optimize health and experience more vitality (supplements for specific conditions)
- 3. Replace unhealthy stuff with good stuff
 - Combine health with joy and enjoyment
 - > Integration in daily life \rightarrow Long term compliance
 - Effective prevention and therapy
 - With sales of products go:
 Dr. Jacobs eating plan with receipies and effective life style changes



How to succeed? Dr. Jacob's concept: simple, effective, holistic

Our solutions:

- Healthy coffees: Chi-Cafe fiber for bowel movements, alkaline minerals & plant extracts. B12 (ReiChi, Chi-Cafe free)
- Alkaline Formulas: the essential mineral supplement after 50.
- Healthy beverages: Aronia-Elixier, Lactacholin, Lactirelle
- Flavochino: finally say YES to cocoa and chocolate!
- DHA+EPA vegan TocoProtect: Gourmet olive oil with omega-3-fatty acids and tocopherols
- Vitamin D3 and K2 oils: easy to take and great to absorb
- AminoBase: all-round meal replacement for weight reduction
- Pomegranate Elixir: heart, blood pressure, prostate, breast
- Eating plan and recipies, life style changes



- Rich in soluble fiber from acacia fiber (exception ReiChi)
 Approx. 10 g / 3 cups ≈ 1/3 of the DGE recommendation
 - Gentle for the stomach and intestines
- With caffeine from coffee + guarana
 - > Gentle, longer lasting stimulating effect as caffeine from coffee
- Contains minerals (calcium from acacia fibers, magnesium)
- > Plant extracts \rightarrow polyphenols (Chi-Cafe balance)
- Formula balances negative effects of coffee (Mineral losses, gastrointestinal discomfort, headache, nervousness etc.)
- Delicious!



Is coffee acidifying the body?
 PRAL-value of coffee is alkaline, but
 Caffeine raises mineral excretion
 In the long term, common coffee turns the body acidic, decreases bone density and increases osteoporosis risk! (Hallström *et al.*, 2013)

≻ Chi-Cafe

- Contains caffeine, but also
- > Contains minerals (e.g. calcium from acacia fibers)

 \rightarrow Chi-Cafe compensates the mineral loss due to caffeine

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Coffee – health effects

- Stimulates nervous system, increases attention and concentration
- Increases physical performance, especially endurance
- Decreases risk for various diseases:
 - Parkinson and Alzheimer's dementia (-31 %/-65 % for 3-5 cups/day)
 - Breast and prostate cancer
 - Cirrhosis
 - Asthma attacks
 - Diabetes mellitus type 2
- Negative Effects:
 - Loss of Calcium and Magnesium \rightarrow bone loss
 - Headache, nervousness and gastrointestinal problems possible

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Acacia fiber

Soluble fiber

Serves as food for bifidobacteria and lactobacillus

 Fermentation to short-chain fatty acids (SSFA) such as butyrate → Nutrient for intestinal mucosa, immune modulator

Contains Arabinogalactan

- Anti-inflammatory, anti-allergic; activates natural killer cells
- Improves intestinal barrier and thus counteracts leaky gut
- Protects the gastrointestinal mucosa from coffee irritants
- Increases satiety, helps to reduce abdominal fat
- Regulates digestion, increases stool volume



Der sanfte wachmacher für Genießer

Reishi (mushroom of longevity) is the most important healing mushroom in TCM, a natural antihistamine and adaptogen ⁶⁷

How to start? Add good stuff! Have fun!

- Breakfast: oatmeal, soy milk, linseed, apples, Pomegranate elixir
- Lunch: healthy fillers first: salad with broccoli seeds and elixir or soup with broccoli seeds and elixir
- Dessert, for example: Pomegranate elixir with soy milk
- Supper: Superfood pesto with wholemeal bread















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A culinary adventure: Eat your fill of Dr. Jacobs plate





Your wife is the key!





Hypertension and medication gone, carotid artery rejuvenated

Medication for hypertension (untreated over 160/90 mm HG up to 200 mm HG systolic) over 10 years: Candesartan (up to 32 mg daily), Olmetec, Aliskeren, Nitrendipin. Side effects: polyneuropathy, muscle pain, severe fatigue, etc.

Now normal blood pressure without medication, no SE.

→ Plaque on carotid bifurcation (2.7 mm) removed → Intima Media thickness: reduced from 1.7 to 1 mm

www.dr-manfred-gessler.de



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Dr. Jacobs Essentials Pesto

- 1 Tbsp. ground broccoli seeds (glucosinolates)
- 1 heaped Tbsp. ground linseeds (*lignans, fiber, omega-3-fatty acids*)
- 30 g tomato paste without salz (*lycopin*)
- 1 Tbsp. linseed oil (omega-3-fatty acids)
- 2 Tsp. curcuma powder or 1 capsule Curcumin K2
- 20 ml Pomegranate elixir (mediterranean) (highly concentrated polyphenols)
- Optional: 1 drop Vitamin D3 oil
- Optional: 5 g horseradish, spicy (glucosinolates und myrosinase)



Pomegranate soy yogurt

- 20 ml Pomegranate elixir
- 100 ml soy drink

Dr. Jacob's pomegranate ketchup

- 20 ml Pomegranate elixir
- 30 g tomato paste







What is unique about:

Dr. Jacob's pomegranate products


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Health Effects

- Potassium:
 - contributes to the maintenance of normal blood pressure

• Pomegranate polyphenols:

- Antioxidative
- Antiinflammatory
- Protection of heart and blood vessels
 - Reduction of blood vessel deposits
 - Cholesterol-lowering
 - Anti-hypertensive
- Protection from Alzheimer's disease, beneficial in MCI (mild cognitive impairment)
- Antibacterial, antiviral
- Anti-cancerous
- Anti-estrogenic





What is unique about Dr. Jacob's pomegranate products?

- Highly concentrated in pomegranate polyphenols
 Tannins, flavonoids (e.g. punicalagin, ellagic acid)
- Standardized, stable polyphenol content
- Strict quality controls: authenticity, pesticides and polyphenols
- Patented manufacturing process using live fermentation → less sugar
- Caps: Freeze-drying
- Elixir: Delicious taste for daily relish
 - \rightarrow fruity astringent flavor as quality feature
 - \rightarrow easy integration into everyday life





Live fermentation

- Bioavailability of pomegranate polyphenols depends on composition of the intestinal flora
- Fermentation with selected microorganisms as natural pre-digestion
 - Polyphenols are released from larger compounds
 - Improves utilization and bioactivity of pomegranate polyphenols
 - Degradation of fruit sugar
- The process of live fermentation was developed by Dr. L. M. Jacob in 2004 and registered as an EU patent.

Live fermentation

pomegranate direct juice (250 ml)

pomegranate elixir (20 ml)



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SUGAR



Fermented pomegranate polyphenols

- Inhibit hormone-refractory prostate cancer cells (Albrecht *et al.*, 2004; Lansky *et al.*, 2005a und b)
- Inhibit neoplasm of tumor vessels (Toi *et al.*, 2003)
- Inhibit breast cancer cells, antiestrogenic (Kim *et al.*, 2002)





Heat dried

Freeze-drying

- After fermentation the juice is deep-frozen and dehydrated at max. 37°C under vaccuum
- Soluble powder with a large surface for optimal intestinal resorption
- Freshness quality and the natural spectrum of plant compounds is optimally preserved
- Conventional heat-drying: Polyphenols become difficult-to-absorb polymeric compounds

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Pomegranate polyphenols inhibit cancer in at least 14 ways





Pomegranate inhibits inflammatory processes



Pomegranate polyphenols inhibit activation of NF-KappaB

(Shukla et al., 2008 b; Khan et al., 2007a und b, Syed et al., 2006; Huang et al., 2005; Ahmed et al., 2005; Afaq et al., 2005a und b; Schubert et al., 2002)

Inflammatory cascade initially regulated, excessive inflammatory reaction prevented

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Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-kappaB-dependent mechanism.

Constitutive nuclear factor-kappaB (NF-kappaB) activation is observed in androgenindependent prostate cancer and represents a predictor for biochemical recurrence after radical prostatectomy. Dietary agents such as pomegranate extract (PE) have received increasing attention as potential agents to prevent the onset or progression of many malignancies, including prostate cancer. Here, we show that PE inhibited NF-kappaB and cell viability of prostate cancer cell lines in a dose-dependent fashion in vitro. Importantly, maximal PE-induced apoptosis was dependent on PE-mediated NF-kappaB blockade. In the LAPC4 xenograft model, PE delayed the emergence of LAPC4 androgen-independent xenografts in castrated mice through an inhibition of proliferation and induction of apoptosis. Moreover, the observed increase in NF-kappaB activity during the transition from androgen dependence to androgen independence in the LAPC4 xenograft model was abrogated by PE. Our study represents the first description of PE as a promising dietary agent for the prevention of the emergence of androgen independence that is driven in part by heightened NF-kappaB activity.

<u>Rettig MB, Heber D, An J, Seeram NP, Rao JY, Liu H, Klatte T, Belldegrun A, Moro A, Henning SM, Mo D,</u> <u>Aronson WJ, Pantuck A.</u> 1: Mol Cancer Ther. 2008 Sep;7(9):2662-71



Clinical studies: Pomegranate against prostate cancer

- Study with 48 patients over 33 months (Pantuck *et al.*, 2006)
 570 mg pomegranate polyphenols (in pomegranate juice): PSA doubling time increased from 15,6 to 54,7 months
- Study with 104 patients over 18 months with POMX PSADT increased from 11,9 to 18,5 months (Paller *et al.*, 2013)
- Double-blind study with 183 patients, POMX (Pantuck *et al.*, 2015): Verum and placebo extend PSA doubling time. *MnSOD* AA subgroup: significantly extended from 13,6 to 25,6 months.
- Study with 203 patients over 6 months (Thomas *et al.*, 2013) Extracts of pomegranate, green tea, broccoli and turmeric: PSA increase 14,7% (verum) vs. 78,5% (placebo)

Typical feedback, stable PSA over many years

- Herr X betont nochmal, er hat den Krebs besiegt. Die Ärzte wundern sich, er braucht nicht bestrahlt zu werden. Nimmt schon seit vielen Jahren Granaprostan. Werte super und fühlt sich topfit. "Granaprostan ist schuld daran, daß ich so gute Werte habe."
- Frau Y ist von unserem Granatapfel-Elixier begeistert. Ihr Mann nimmt es seit 3 Jahren. Urologe sagt super!
- Schon lange empfiehlt er die Granatapfel-Elixiere f
 ür seine Krebspatienten. Haupts
 ächlich Brustkrebs. Er hat Prostatakrebspatienten in Behandlung und das Elixier ist "super toll". Er verschreibt vielen auch vorbeugend, seiner Meinung auch am besten. Bei Brustkrebs: Basistherapie dann nach 5 Jahren Granatapfel-Elixier.
- SHGler lebt nach "Krebszellen mögen keine Himbeeren" und findet unser Elixier ausgezeichnet. Er ist Molekularbiologe und und It. Ärzte schon 5 Jahre tot...Ist schon seit vielen Jahren Kunde und bestellt regelmäßig Granatapfel-Elixier.

Pomegranate polyphenols in breast cancer?

- Have an anti-carcinogenic effect at all stages of carcinogenesis
- Reduce the expression of estrogen receptors in breast cancer tissue
- Block the carcinogenic estrogen receptor alpha (ERalpha)
- Act as aromatase inhibitors and thus reduce estrogen formation
- Inhibit growth of estrogen receptor-positive and -negative breast cancer cells and breast cancer stem cells

Pomegranate effects on heart and circulation





Pomegranate and dementia

- Fruit and vegetable juices reduce risk for Alzheimer's disease by 76% (Dai *et al.*, 2006) due to
 - High polyphenol content
 - High potassium content
- Pomegranate polyphenols reduce beta-amyloid deposits in mouse brains by half (Hartman *et al.*, 2006) due to
 - Antioxidative effects
 - Influence on cell signalling and enzymatic systems
 - Regulation of gene expression
- Potassium-sparing diuretics reduce risk for Alzheimer's disease by 74% (Khachaturian *et al.*, 2006) → potassium levels up



Dosage

- In studies pomegranate polyphenols at a daily dose of 600 mg (as gallic acid equivalent) mostly show effects
- For prevention: 300 mg/day
- Daily dose should be taken at once
- Not on empty stomach in the morning
- Pomegranate Elixir can be taken with sparkling water, soy milk or tomatoe pulp





Pomegranate products

Pure pomegranate polyphenols

- Pomegranate elixir
- Grana*forte*
- GranaProstan *ferment*

Products with additional benefits

- Pomegranate elixir
 mediterranean
- Grana*med*
- GranaCor



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Pomegranate elixir

Filled with polyphenols and great taste

- The original premium quality since 2004
- Pure fruity, astringent pomegranate taste
- Excellent price-polyphenol ratio
- 25-fold concentrated in polyphenols from the whole fruit: 20 ml contain: 720 mg polyphenols (300 mg punicalagins)
- Over 80 % less sugar than pomegranate juice at the same polyphenolic content
- High bioactivity due to patented live fermentation







Grana*forte*

Highly concentrated in polyphenols and punicalagins

- Highly concentrated: approx. 500 mg polyphenols incl. 300 mg punicalagin per serving
- 90 % less sugar than pomegranate juice at the same polyphenolic content
- **High bioactivity** due to patented live fermentation
- Best price-polyphenolic ratio





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GranaProstan ferment

With pomegranate juice extract

- High content in polyphenols (720 mg/4 caps) and punicalagin (340 mg / 4 caps)
- High bioactivity due to patented live fermentation
- Optimal freshness quality due to gentle freezedrying
- Plant-based capsule shell
- Perfect for travellers



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Pomegranate elixir mediterranean

Mediterranean blend for healthy blood flow

- Patented tomato extract for the blood flow
- live fermented pomegranate polyphenols
- Polyphneol extract from red wine grapes



Thrombocytes get "sticky" in situations of stress, sports, overweight and high cholesterol, activate blood coagulation and decrease blood flow.





Tomato extract WSTC

- WSTC keeps blood platelets smooth and thus counteracts undesirable clumping in blood vessels
- Does not affect normal blood coagulation after injury
- The effect occurs in 97 % of people within 1.5 hours and maintains for 24 hours when taken regularly
- Effective daily dose:
 - 20 ml of Pomegranate elixir *mediterranean* (3 g WSTC I) or
 - 4 capsules of Grana*med* (150 mg WSTC II)
 - Take in each product with a big glass of water



Dr. Jacob's pomegranate products – comparison (I)

	Pomegranate elixir	Grana <i>forte</i>	GranaProstan ferment	Pomegranate elixier <i>mediter-</i> <i>ranean</i>	Grana <i>med</i>	GranaCor
Special ingredients						
Polyphenols*	720 mg	500 mg	720 mg	800 mg	650 mg	720 mg
- thereof punicalagin	300 mg	300 mg	340 mg	245 mg	240 mg	340 mg
Polyphenols live fermented?	partly	partly	100 %	partly	100 %	100 %
Elderberry concentrate	\checkmark	✓				
Tomato concentrate				✓	✓	
Extract from red wine grapes				✓	✓	
Mediterranean plant extracts					✓	
Lactic acid		\checkmark				
Vitamins						
Vitamins D, E						\checkmark
Vitamins B1, B6, B12, folic						\checkmark
acid						
Minerals					1	
Potassium	✓			✓		
Selenium						\checkmark

*Content per max. daily portion

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Delicious pomegranate recipes



Dr. Jacob's pomegranate ketchup

- 20 ml Pomegranate elixir
- 30 g tomato paste

Granatapfel-Eline Decetement

Dr. Jacob's Essentials Pesto

- 1 level Tbsp. Broccoli seeds
- 1 heaped Tbsp. linseeds
- 30 g tomato paste
- 1 Tbsp. linseed oil
- 2 Tsp. curcuma powder or 1 capsule Curcumin K2
- 20 ml Pomegranate elixir (*mediterranean*)
- Optional: 1 drop Vitamin D3 oil
- Optional: 5 g horseradish, spicy

Pomegranate soy yogurt

- 20 ml Pomegranate elixir
- 100 ml soy drink





Broccoli sulforaphan against cancer

- Sulforaphane and its metabolites are the principal bioactive phytochemicals from broccoli and broccoli sprouts
- Glucoraphane is cleaved by the endogenous plant enzyme myrosinase into sulforaphane (SFN)



• SFN shows opposite effects in normal and cancer cell: while in normal cells it has protective actions, in cancer cells it works anti-cancerogenic.



Sulforaphane against prostate cancer cells



Anti-carcinogenic effects of sulforaphane (modified according to Zhang and Tang, 2007)

2.6.2018: 878 hits on pubmed for « sulforaphane cancer »

Suppression of the inflammatory response, apoptosis and growth arrest

Sulforaphane

- inhibits the Akt signaling (often hyperactive in prostate cancer)
- decrease pro-survival signaling by mTOR, Akt and NF*kappa*B
- changes in gene expression (blue arrow) that trigger growth arrest and apoptosis.
- The expression of cell cycle controlling proteins (e.g. p21, p27, and CDK6) is altered to effect growth arrest, and apoptosis.
- upregulates Nrf2 which has preventive and therapeutic effects on inflammatory diseases.



Selected non-epigenetic effects of sulforaphane on prostate cancer cells. *(modified according to Watson et al. 2013)*



Epigenetic modulator activity

Histone deacetylases (HDACs) regulate the expression and activity of numerous proteins involved in both cancer initiation and cancer progression.

Sulforaphane (SFN) :

 inhibits histone deacetylase, which eventually leads to the increase of transcription of pro-apoptotic factors, such as Bax, Bad, and p21, and subsequently apoptosis



The role of Sulforaphane in cancer chemoprevention and health benefits: a mini-review *(Mokhtari, 2018)*

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The anti-angiogenesis, anti-metastasis and autophagy activities of SFN

- a. Sulforaphane (SFN) inhibits transcription factors hypoxia inducible factor (HIF)-1alpha, nuclear factor-kappaB (NFkB), and proto-oncogene myc (c-Myc), resulting in the downregulation of key angiogenic and metastatic regulators, vascular endothelial growth factor (VEGF) and matrix metallopeptidase 9 (MMP-9), and thus, the reduction of angiogenic and metastatic potential.
- SFN induces the recruitment and increases the expression of LC3 to autophagosomes, thus, increasing the activation of the autophagy pathway



The role of Sulforaphane in cancer chemoprevention and health benefits: a mini-review (*Mokhtari, 2018*)



Hormonal blockade

- A study on prostate cancer cells (Khurana et al., 2016) showed that sulforaphane can be useful in cases of hormonal blockade.
- The simultaneous treatment of the cells with sulforaphane and antiandrogens (bicalutamide, enzalutamide) strengthened the anti-proliferative effect of antiandrogens and reduced the expression of the PSA gene.
- The migration of prostate cancer cells has also been reduced. Sulforaphane even reduced the androgen receptors present.

A phase II study of sulforaphane-rich broccoli sprout extracts in men with recurrent prostate cancer (Alumka *et al.* 2015)

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- 20 patients (prostate cancer): 35 mg of extracts rich in sulforaphane for max 20 weeks
- Results: 7 patients had a reduction in PSA of 3 to 20% or even more than 50% in one patient.
- PSA doubling time (PSADT) increases : 6.1 months before treatment vs 9.6 months after treatment

Double-blind, placebo-controlled trial with sulforaphane: 78 men ($69 \pm 6 y$) with increasing PSA after prostatectomy

Treatment comprised daily oral administration of 60 mg of a stabilized free sulforaphane for 6 months (M0-M6).

median log PSA slopes were consistently lower in sulforaphane-treated men.

Mean changes in PSA levels between M6 and M0 were significantly lower in the sulforaphane group (+0.099 \pm 0.341 ng/mL) than in placebo (+0.620 \pm 1.417 ng/mL; P = 0.0433).

PSA doubling time was 86% longer in the sulforaphane than in the placebo group (28.9 and 15.5 months, respectively).

PSA increases >20% at M6 were significantly greater in the placebo group (71.8%) than in the sulforaphane group (44.4%); P = 0.0163.

Compliance and tolerance were very good.

Sulforaphane effects were prominent after 3 months of intervention (M3-M6).



CURCUMIN: A WIDE RAGE OF USE





Molecular targets upregulated by curcumin

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(Ajaikumar B. Kunumakkaraa, Peetha Ananda, and Bharat B. Aggarwal, © 2008 Elsevie¹⁰5

Curcumin-Phospholipid tested on over 2000 patients **32POSITIVE CLINICAL STUDIES AVAILABLE**

THERAPEUTICAL AREA	N° OF STUDIES
OSTEOARTHRITIS	3
OSTEOPENIA	1
SARCOPENIA	1
EYES DISORDERS	4
SKIN DISORDERS (PSORIASIS)	1
DIABETES	2
LIVER HEALTH (NAFLD)	2
CARDIOVASCULAR HEALTH	1
GASTROINTESTINAL BARRIER	1
AIRWAY inflammation (pediatric)	1
BENIGN PROSTATIC HYPERPLASIA	1
PAIN MANAGEMENT	1
NEUROPATHIES	2
SPORT MEDICINE	2
DIAGNOSTIC (AD)	1

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medizinische Forschung

EVOLUTION OF LIVER FATTY DISORDERS

NAFLD (Nonalcoholic Fatty Liver Disease)



Non Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease in the Western countries, affecting 30% of the general adult population and up to 60-70% in diabetic and obese patients.



Curcumin-Phospholipid against NAFLD

\Rightarrow	Liver enzymes Reduction (p < 0.001)	AST -30% ALT -25%
\Rightarrow	Liver functionality Improvement (ultrasonography)	Hepatic vein flow +24%
	Serum lipids and Uric acid Reduction (p< 0.001)	Total cholesterol-21%Non-HDL-C-26%LDL-C-23%HDL-4%Triglycerides-17%Uric Acid-8%
	BMI Reduction	-3%
	Waist circumference Reduction	-2%

Panahi, Y. et al.. Drug Research 2017; J. Cardiovasc Pharmacol. 2016.


Curcumin-Phospholipid against leaky gut

J Appl Physiol 2017 Sep 21: jap.00515.2017. doi: 10.1152/japplphysiol.00515.2017



Szymanski MC, Gillum TL, Gould LM, Morin DS, Kuennen MR

Short term dietary curcumin supplementation <u>reduces</u> <u>gastrointestinal barrier damage</u> and physiological strain responses during exertional heat stress

Department of Exercise Science, High Point University, High Point, NC 27268 Department of Kinesiology, California Baptist University, Riverside, CA 92504



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Merci pour votre attention!

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